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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/963,875	09/26/2001	Joel F. Habener	17633/1235	9674

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EXAMINER

BELYAVSKIY, MICHAEL A

ART UNIT PAPER NUMBER

1644

DATE MAILED: 11/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/963,875

Applicant(s)

HABENER ET AL.

Examiner

Michail A. Belyavskiy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 September 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39-41, 43, 74, 77-79, 85-107 and 109-111 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39-41, 43, 74, 77-79, 85-107 and 109-111 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 09/07/06 is acknowledged.
2. Claims 39-41, 43, 74, 77-79, 85-107 and 109-111 are pending.
3. Applicant's arguments filed 09/07/06 in conjunction with Declaration of Dr. Habener under 37 C.F.R. 1.131 has obviated the previous rejection of claims 39-41, 43, 74, 77-79, 81, 83 and 85-108 under 35 U.S.C. 103(a) as being unpatentable over WO 00/09666 or WO 02/0861107. Said arguments and declaration demonstrated that the subject matter of claims 39-41, 43, 74, 77-79, 81, 83 and 85-108 was conceived prior to the publication of WO'666 or prior to earliest priority date for WO'107.

In view of the amendment, filed 09/07/06 the following rejection remains:

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 39-41, 43, 77-79 and 85-107 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 9715310 for the same reasons set forth in the previous Office Action, mailed on 03/10/06.

Applicant's arguments filed on 09/07/06 have been fully considered, but have not been found convincing.

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Applicant asserts that : (i) WO'310 does not teach an isolated nestin-positive human pancreatic stem cell, because applicants were unable to produce any viable cells using the method of cell isolation presented in the WO'310 application; (ii) Declaration under 37 CFR 1.132 by Dr. Elizabeth Abraham stated that culturing conditions for obtaining isolated nestin-positive cells of the instant application and culture condition of WO'310 are substantially different.

Contrary to Applicant assertion, it is the Examiner position that that WO'310 teaches a viable cells. At page 16 of WO'310, it is clearly stated that "we have been able to propagate and expand islet-producing cultures". Figures 1-2 and 4 clearly shows a viable morphology of the obtained isolated cells. Moreover, the fact that said cells are viable is further supported by their in vivo studies wherein said isolated cells were capable to reverse IDD when implanted into NOD mice (see page 16 of US'310).

With regards to the issue that applicants were unable to produce any viable cells using the method of cell isolation presented in the WO'310 application.

The fact that applicants were unable to produce any viable cells does not neglect the teaching of WO'310 itself. It is well settled that "Even if a reference discloses an inoperative device, it is prior art for all that it teaches". *Beckman Instruments v LKB Produkter AB*, 892 F.2d 1547,1551,13 USPQ2d 1301,1304 (Fed.Cir. 1989).

However, in the instant case it is noted that , as acknowledged in Declaration by Dr. Elizabeth Abraham, filed on 09/07/2006, WO' 310 protocol used Click's EHAA medium , while in experiment conducted by Dr. Elizabeth Abraham, said medium has been substituted to DMEM. One skill in the art would know that culturing condition and specially growth medium, CO₂ content, humidity and temperature are essential for the successful growth and maintaining of cell culture. Even little changes in any of said conditions can effect the viability of the cultured cells. The cells that can be propagated or maintained in one culture medium, would not grow in a different culture medium. One skill in the art would expect that substituting Click's EHAA medium with DMEM medium would affect the outcome of the experiment. It is also noted that in the instant Specification, Applicants were using RPMI 1640 medium rather than DMEM medium for isolation of nestin-positive cells.

Further, in Declaration by Dr. Elizabeth Abraham, filed on 09/07/2006 it is stated that WO'310 does not teach that cells are cultured in the media in the presence of glucose, high serum and growth factors. Applicant's attention is respectively drawn to overlapping pages 14 and 15 of WO'310. It is explicitly stated that subsequent culture phases employ media supplemented with normal serum, glucose and growth factors. In case of human islet cells the medium is supplemented with normal human serum.

Thus, it is the Examiner position that WO'310 teaches an isolated viable nestin-positive human pancreatic stem cells that are not a neural stem cells that can differentiate to form insulin-producing cells. (see entire document, pages 8 ,10, 13 in particular). WO'310 teaches a

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pharmaceutical composition comprising said cells in cultured media or in PBS, that is a physiologically compatible carrier. (see pages 13 and 14 in particular). WO'310 teaches several methods of isolating pancreatic stem cells comprising steps of removing a pancreatic islet from the donor and separating stem cells from plurality of cells (see overlapping pages 22 - 24, in particular). The method of isolating said cells is substantially similar to that used by applicant (see overlapping pages 22-24 in particular). While WO'310 does not specifically teach that these cells are GLP-1R-positive cells, said cells would obviously be GLP-1R-positive cells, since the cell population taught by WO'310 is identical to that claimed in the instant application. It is noted that WO'310 does not explicitly teaches an isolated nestin-positive human pancreatic stem cells, wherein said cells are at least 30 % or 40% or 60 % or 70 % or 80 % or 85 % or 90 % or 99 % pure as claimed . However, at the time the invention was made one skilled in the art would know how to obtained an isolated population of human pancreatic stem cells wherein said cells are at least 30 % or 40% or 60 % or 70 % or 80 % or 85 % or 90 % or 99 % pure as claimed. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, preparing an isolated cell composition that would be at least 30 % or 40% or 60 % or 70 % or 80 % or 85 % or 90 % or 99 % pure involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

Moreover, it is noted that Applicant acknowledge that at the time the invention was made one skilled in the art will appreciate that a variety of separation strategies based on immunophenotyping methodologies such as surface coated antibody panning, fluorescent antibody tagging for physical isolation, flow cytometric sorting, immunomagnetic bead and particle selection and counterselection can be used to obtained isolated distinct population of nestin+ cells (see Applicant's argument mailed on 12/27/05, overlapping pages 19-20 in particular).

Claim 43 is included because the claimed functional limitation would be obvious properties of an isolated cells taught by WO'310 because the referenced cells are the same as claimed and would obviously be able to differentiates to insulin-producing cells. Said insulin -producing cells are the only beta cells to which nestin-positive human pancreatic stem cells can differentiate in the absence of evidence of structural difference.

Claims 77-79 and 105-107 are included because the instant claims are drawn to a product, i.e. to an isolated nestin-positive human pancreatic stem cells. Patentability of the product, i.e. isolated, nestin-positive stem cells does not depends on the method of production or a source from which said cells were isolated in the absence of evidence of structural difference. *In re Thrope*, 227 USPQ 964,966 (Fed. Cir. 1985). See MPEP 2113.

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The following new grounds of rejection is necessitated by the amendment filed 09/07/06

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 74 and 109-11 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 9715310

WO'310 teaches an isolated viable nestin-positive human pancreatic stem cells that are not a neural stem cells that can differentiate to form insulin-producing cells. (see entire document, pages 8,10, 13 in particular). WO'310 teaches a pharmaceutical composition comprising said cells in cultured media or in PBS, that is a physiologically compatible carrier. (see pages 13 and 14 in particular). WO'310 teaches several methods of isolating pancreatic stem cells comprising steps of removing a pancreatic islet from the donor and separating stem cells from plurality of cells (see overlapping pages 22 -24, in particular). The method of isolating said cells is substantially similar to that used by applicant (see overlapping pages 22-24 in particular). While WO'310 does not specifically teach that these cells are GLP-1R-positive cells, said cells would obviously be GLP-1R-positive cells, since the cell population taught by WO'310 is identical to that claimed in the instant application. Mere recognition of latent properties in the prior art (i.e. nestin-positive cell is also GLP-1R positive) does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979).

Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Since the office does not have a laboratory to test the reference isolated nestin-positive human pancreatic stem cells, it is applicant's burden to show that the reference nestin-positive human pancreatic stem cells do not have the functional limitation as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

The reference teachings anticipate the claimed invention.

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8. No claim is allowed

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskiy whose telephone number is 571/ 272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



MICHAEL BELYAVSKIY, PH.D.
PATENT EXAMINER

11/3/06